```
=>

=> fil reg
FILE 'REGISTRY' ENTERED AT 12:08:41 ON 05 JAN 2004
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:     4 JAN 2004  HIGHEST RN 634148-43-9
DICTIONARY FILE UPDATES:    4 JAN 2004  HIGHEST RN 634148-43-9

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d que stat l5
L1              SCR 1568
L2              STR

H2N-- CH- G1-- S
  1   2   3   4


REP G1=(1-2) C
NODE ATTRIBUTES:
CONNECT IS X2  RC AT   4
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS   4

STEREO ATTRIBUTES: NONE
L3   (     63158)SEA FILE=REGISTRY SSS FUL L2 AND L1
L4              STR

H2N-- CH- G1-- S-- G2       S-- Ak-- NH2
  1   2   3   4   5       @6   7   8


REP G1=(1-2) C
VAR G2=H/6
NODE ATTRIBUTES:
CONNECT IS X2  RC AT   4
CONNECT IS X2  RC AT   6
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS M2-X3 C  AT   7

GRAPH ATTRIBUTES:
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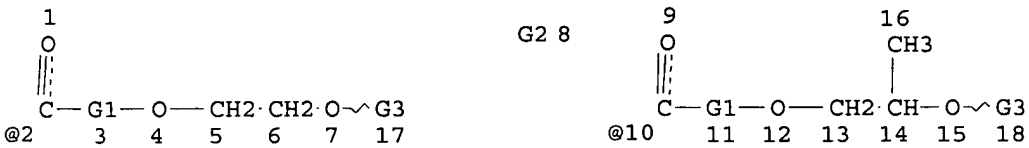
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 8

STEREO ATTRIBUTES: NONE
L5 21545 SEA FILE=REGISTRY SUB=L3 SSS FUL L4

100.0% PROCESSED 63158 ITERATIONS 21545 ANSWERS
SEARCH TIME: 00.00.04

=> d que stat l10
L6 (89145)SEA FILE=REGISTRY ABB=ON PLU=ON C2H4O
L7 (50015)SEA FILE=REGISTRY ABB=ON PLU=ON C3H6O
L8 (121153)SEA FILE=REGISTRY ABB=ON PLU=ON L6 OR L7
L9 STR



Ak @19

REP G1=(0-2) CH2
VAR G2=10/2
VAR G3=H/19
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 19
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 19

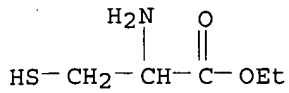
STEREO ATTRIBUTES: NONE
L10 17972 SEA FILE=REGISTRY SUB=L8 SSS FUL L9

100.0% PROCESSED 102611 ITERATIONS 17972 ANSWERS
SEARCH TIME: 00.00.02

=> d que l11;d l11 1-2
L11 2 SEA FILE=REGISTRY ABB=ON PLU=ON "CYSTEINE, ETHYL ESTER"/CN

L11 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN
RN 69685-04-7 REGISTRY
CN **Cysteine, ethyl ester (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN DL-Cysteine, ethyl ester
FS 3D CONCORD
DR 89830-80-8

MF C5 H11 N O2 S
CI COM
LC STN Files: BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, CHEMINFORMRX, CHEMLIST, EMBASE, GMELIN*, IFICDB, IFIPAT, IFIUDB, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

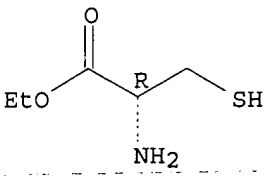


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

9 REFERENCES IN FILE CA (1907 TO DATE)
9 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L11 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2004 ACS on STN
RN 3411-58-3 REGISTRY
CN L-Cysteine, ethyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Cysteine, ethyl ester, L- (7CI, 8CI)
OTHER NAMES:
CN **Cysteine, ethyl ester**
CN Ethyl cysteinate
CN Ethyl L-cysteinate
FS STEREOSEARCH
MF C5 H11 N O2 S
CI COM
LC STN Files: BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMINFORMRX, CHEMLIST, DDFU, DRUGU, EMBASE, GMELIN*, IFICDB, IFIPAT, IFIUDB, MEDLINE, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

430 REFERENCES IN FILE CA (1907 TO DATE)
23 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
430 REFERENCES IN FILE CAPLUS (1907 TO DATE)
9 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> d que l33;d l33

L33 1 SEA FILE=REGISTRY ABB=ON PLU=ON MERCAPTAMINE/CN

L33 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 60-23-1 REGISTRY
CN Ethanethiol, 2-amino- (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN β-Aminoethanethiol
CN β-Aminoethylthiol
CN β-MEA
CN β-Mercaptoethylamine
CN 1-Amino-2-mercaptoethane
CN 2-Amino-1-ethanethiol
CN 2-Aminoethanethiol
CN 2-Aminoethyl mercaptan
CN 2-Mercaptoethanamine
CN 2-Mercaptoethylamine
CN Becaptan
CN Cysteamine
CN Cysteinamine
CN Decarboxycysteine
CN L 1573
CN Lambraten
CN Lambratene
CN MEA
CN MEA (mercaptan)
CN Mercamin
CN Mercamine
CN Mercaptamin
CN **Mercaptamine**
CN Mercaptoethylamine
CN Merkamin
CN NSC 647528
CN Riacon
CN Thioethanolamine
CN WR 347
FS 3D CONCORD
DR 139720-70-0
MF C2 H7 N S
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DETHERM*, DRUGU, EMBASE, GMELIN*, HODOC*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PIRA, PROMT, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

$H_2N-CH_2-CH_2-SH$

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5010 REFERENCES IN FILE CA (1907 TO DATE)

276 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
5012 REFERENCES IN FILE CAPLUS (1907 TO DATE)
75 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

```
=> fil caplus
FILE 'CAPLUS' ENTERED AT 12:09:26 ON 05 JAN 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 5 Jan 2004  VOL 140 ISS 2
FILE LAST UPDATED: 4 Jan 2004  (20040104/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

=> d que nos l38
L1              SCR 1568
L2              STR
L3   (     63158)SEA FILE=REGISTRY SSS FUL L2 AND L1
L4              STR
L5         21545 SEA FILE=REGISTRY SUB=L3 SSS FUL L4
L6   (     89145)SEA FILE=REGISTRY ABB=ON  PLU=ON  C2H4O
L7   (     50015)SEA FILE=REGISTRY ABB=ON  PLU=ON  C3H6O
L8   (    121153)SEA FILE=REGISTRY ABB=ON  PLU=ON  L6 OR L7
L9              STR
L10        17972 SEA FILE=REGISTRY SUB=L8 SSS FUL L9
L11            2 SEA FILE=REGISTRY ABB=ON  PLU=ON  "CYSTEINE, ETHYL ESTER"/CN
L12        46766 SEA FILE=CAPLUS ABB=ON  PLU=ON  COLLAGENS/CT
L13        66163 SEA FILE=CAPLUS ABB=ON  PLU=ON  L5
L14        17556 SEA FILE=CAPLUS ABB=ON  PLU=ON  L10
L15          525 SEA FILE=CAPLUS ABB=ON  PLU=ON  L12 AND L13
L16          118 SEA FILE=CAPLUS ABB=ON  PLU=ON  L12 AND L14
L18         1193 SEA FILE=CAPLUS ABB=ON  PLU=ON  L12 (L) (RCT OR RACT)/RL
L23          438 SEA FILE=CAPLUS ABB=ON  PLU=ON  L11
L25         1225 SEA FILE=CAPLUS ABB=ON  PLU=ON  L12 (L) REACTION?/OBI
L26         1685 SEA FILE=CAPLUS ABB=ON  PLU=ON  L25 OR L18
L27           51 SEA FILE=CAPLUS ABB=ON  PLU=ON  L26 AND (L15 OR L16)
L28            2 SEA FILE=CAPLUS ABB=ON  PLU=ON  L27 AND L23
L29        92653 SEA FILE=CAPLUS ABB=ON  PLU=ON  MERCAP?/OBI
L30        52282 SEA FILE=CAPLUS ABB=ON  PLU=ON  THIOL?/OBI
L31       130268 SEA FILE=CAPLUS ABB=ON  PLU=ON  L29 OR L30
L32            7 SEA FILE=CAPLUS ABB=ON  PLU=ON  L31 AND L27
L33            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  MERCAPTAMINE/CN
L34         5026 SEA FILE=CAPLUS ABB=ON  PLU=ON  L33
L35            4 SEA FILE=CAPLUS ABB=ON  PLU=ON  L27 AND L34
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disregard highlighting

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L36           9 SEA FILE=CAPLUS ABB=ON  PLU=ON  L35 OR L32 OR L28
L37          17 SEA FILE=CAPLUS ABB=ON  PLU=ON  L27 AND 63/SX,SC
L38          19 SEA FILE=CAPLUS ABB=ON  PLU=ON  L37 OR L36


=> d .ca hitstr l38 1-10

L38  ANSWER 1 OF 19  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2003:609843  CAPLUS
DOCUMENT NUMBER:          139:169326
TITLE:                    Device and methods for initiating chemical reactions
                          and for the targeted delivery of drugs or other agents
INVENTOR(S):              Ueberle, Friedrich
PATENT ASSIGNEE(S):       Germany
SOURCE:                   U.S. Pat. Appl. Publ., 19 pp.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     US 2003147812      A1   20030807       US 2002-316273   20021211
     EP 1319423         A3   20031008       EP 2002-27643    20021211
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
PRIORITY APPLN. INFO.:                    US 2001-339285P  P  20011211
AB   The present invention is directed to methods and apparatus for the targeted
     initiation or deactivation of chemical reactions by an acoustic energy source
     in a host.  Methods and apparatus for the targeted delivery of drugs,
     diagnostic agents and other compds. using an acoustic energy source are
     also provided.
IC   ICM  A61N001-30
NCL  424009520; 604020000
CC   63-6 (Pharmaceuticals)
IT   Agglutinins and Lectins
     Antibodies
       Collagens, biological studies
     DNA
     Elastins
     Glycoproteins
     Hormones, animal, biological studies
     Integrins
     Interferons
     Interleukin 1
     Interleukin 10
     Interleukin 11
     Interleukin 12
     Interleukin 2
     Interleukin 3
     Interleukin 4
     Interleukin 5
     Interleukin 6
     Interleukin 7
     Interleukin 8
     Interleukin 9
     Lymphokines
     Lymphotoxin
     Monosaccharides
```

Nucleosides, biological studies
Nucleotides, biological studies
Peptides, biological studies
Platelet-derived growth factors
Polymers, biological studies
Polynucleotides
Polysaccharides, biological studies
Porphyrins
Prostaglandins
Proteins
RNA
Retinoids
Ricins
Steroids, biological studies
Transforming growth factors
Tumor necrosis factors
Vitamins
cDNA
mRNA
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(device and methods for initiating chemical **reactions** and for targeted delivery of drugs or other agents)

IT 50-02-2, Dexamethasone 50-03-3, Hydrocortisone acetate 50-04-4, Cortisone acetate 50-23-7, Hydrocortisone 50-24-8, Prednisolone 50-28-2, Estradiol, biological studies 50-33-9, Phenylbutazone, biological studies 50-56-6, Oxytocin, biological studies 50-78-2, Aspirin 51-05-8, Procaine hydrochloride 51-61-6, Dopamine, biological studies 52-21-1, Prednisolone acetate 52-53-9, Verapamil **52-67-5**, Penicillamine 53-03-2, Prednisone 53-36-1, Methylprednisolone acetate 53-86-1, Indomethacin 54-05-7, Chloroquine 54-85-3, Isoniazid 55-63-0, Nitroglycerin 56-75-7, Chloramphenicol 57-27-2, Morphine, biological studies 57-30-7, Phenobarbital sodium 57-43-2, Amobarbital 57-83-0, Progesterone, biological studies 57-94-3, Tubocurarine chloride 58-22-0, Testosterone 58-82-2, Bradykinin 59-02-9, α-Tocopherol 59-30-3, Folic acid, biological studies 60-54-8, Tetracycline 61-32-5, Methicillin 61-33-6, Penicillin G, biological studies 61-68-7, Mefenamic acid 64-43-7, Amobarbital sodium 65-29-2, Gallamine triethiodide 65-49-6, Para-aminosalicylic acid 66-79-5, Oxacillin 67-78-7, Triamcinolone diacetate 67-97-0, Cholecalciferol 68-19-9, Cyanocobalamine 68-41-7, Cycloserine 69-53-4, Ampicillin 69-72-7D, Salicylic acid, derivs. 70-18-8, Glutathione, biological studies 71-27-2, Succinylcholine chloride 71-63-6, Digitoxin 71-73-8, Thiopental sodium 73-78-9, Lidocaine hydrochloride 76-25-5, Triamcinolone acetonide 76-57-3, Codeine 76-74-4, Pentobarbital 76-99-3, Methadone 77-02-1, Aprobarbital 77-21-4, Glutethimide 78-11-5, Pentaerythritol tetranitrate 79-81-2, Retinol palmitate 80-08-0, Dapsone 83-43-2, Methylprednisolone 87-08-1, Penicillin V 87-33-2, Isosorbide dinitrate 98-96-4, Pyrazinamide 113-18-8, Ethchlorvynol 114-07-8, Erythromycin 115-44-6, Talbutal 118-42-3, Hydroxychloroquine 123-63-7, Paraldehyde 124-94-7, Triamcinolone 125-02-0, Prednisolone sodium phosphate 125-04-2, Hydrocortisone sodium succinate 125-64-4, Methyprylon 126-07-8, Griseofulvin 126-52-3, Ethinamate 129-20-4, Oxyphenbutazone 130-15-4, 1,4-Naphthalenedione 130-95-0, Quinine 135-16-0 136-47-0, Tetracaine hydrochloride 143-81-7, Butabarbital sodium 147-52-4, Nafcillin 151-73-5, Betamethasone sodium phosphate 154-21-2, Lincomycin 302-17-0, Chloral hydrate 309-36-4, Methohexital sodium 309-43-3, Secobarbital sodium 317-52-2, Hexafluorenium bromide 378-44-9, Betamethasone 443-48-1, Metronidazole 508-99-6, Hydrocortisone cypionate 514-36-3, Fludrocortisone. acetate 525-66-6,

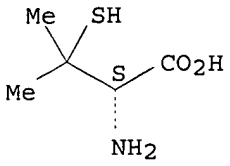
Propranolol 536-33-4, Ethionamide 548-73-2, Droperidol 561-27-3, Heroin 644-62-2 752-61-4, Digitalin 768-94-5, Amantadine 846-50-4, Temazepam 987-24-6, Betamethasone acetate 990-73-8, Fentanyl citrate 1070-11-7, Ethambutol hydrochloride 1172-18-5, Flurazepam hydrochloride 1177-87-3, Dexamethasone acetate 1397-89-3, Amphotericin B 1400-61-9, Nystatin 1404-04-2, Neomycin 1405-37-4, Capreomycin sulfate 1597-82-6, Paramethasone acetate 1722-62-9, Mepivacaine hydrochloride 1867-66-9, Ketamine hydrochloride 2022-85-7, Flucytosine 2375-03-3, Methylprednisolone sodium succinate 2392-39-4, Dexamethasone sodium phosphate 3116-76-5, Dicloxacillin 3385-03-3, Flunisolide 3485-14-1, Cyclacillin 3511-16-8, Hetacillin 3810-74-0, Streptomycin sulfate 3858-89-7, Chloroprocaine hydrochloride 4185-80-2, Methotrimeprazine hydrochloride 4697-36-3, Carbenicillin 5534-09-8, Beclomethasone dipropionate 5536-17-4, Vidarabine 5611-51-8, Triamcinolone hexacetonide 6000-74-4, Hydrocortisone sodium phosphate 6284-40-8D, Meglumine, antimonite complexes 7297-25-8, Erythrityl tetranitrate 7440-15-5, Rhenium, biological studies 7440-24-6, Strontium, biological studies 7440-26-8, Technetium, biological studies 7440-48-4, Cobalt, biological studies 7440-65-5, Yttrium, biological studies 7601-55-0, Metocurine iodide 7681-14-3, Prednisolone tebutate 8029-99-0, Paregoric 9001-12-1, Collagenase 9001-75-6, Pepsin 9001-78-9, Alkaline phosphatase 9002-01-1, Streptokinase 9002-04-4, Thrombin 9002-60-2, Adrenocorticotropic hormone, biological studies 9002-61-3, Human chorionic gonadotropin 9002-72-6, Growth hormone 9002-79-3, Melanocyte stimulating hormone 9004-10-8, Insulin, biological studies 9007-12-9, Calcitonin 9007-92-5, Glucagon, biological studies 9011-97-6, Cholecystokinin 9015-71-8, Corticotropin releasing factor 9039-53-6, Urokinase 9061-61-4, Nerve growth factor 11000-17-2, Vasopressin 11096-26-7, Erythropoietin 13292-46-1, Rifampin 15500-66-0, Pancuronium bromide 15686-71-2, Cephalexin 15687-27-1, Ibuprofen 16009-13-5, Hemin 17598-65-1, Deslanoside 18010-40-7, Bupivacaine hydrochloride 18323-44-9, Clindamycin 20461-54-5, Iodide, biological studies 20830-75-5, Digoxin 21829-25-4, Nifedipine 22204-53-1, Naproxen 22494-42-4, Diflunisal 22916-47-8, Miconazole 24356-66-9 26171-23-3, Tolmetin 26787-78-0, Amoxicillin 28911-01-5, Triazolam 30516-87-1, Azidothymidine 33125-97-2, Etomidate 33507-63-0, Substance P 34787-01-4, Ticarcillin 36322-90-4, Piroxicam 36637-19-1, Etidocaine hydrochloride 36791-04-5, Ribavirin 38194-50-2, Sulindac 38821-53-3, Cephradine 39391-18-9, Cyclooxygenase 42399-41-7, Diltiazem 50370-12-2, Cefadroxil 50700-72-6, Vecuronium bromide 50972-17-3, Bacampicillin 53678-77-6, Muramyldipeptide 53994-73-3, Cefaclor 59277-89-3, Acyclovir 59467-96-8, Midazolam hydrochloride 62031-54-3, Fibroblast growth factor 62229-50-9, Epidermal growth factor 62571-86-2, Captopril 64228-81-5, Atracurium besylate 65277-42-1, Ketoconazole 75847-73-3, Enalapril 76547-98-3, Lisinopril 83869-56-1, Granulocyte-macrophage colony stimulating factor 86090-08-6, Angiostatin 102577-23-1, Neurokinin B 106128-89-6, Senktide 106956-32-5, Oncostatin M 124389-07-7, Muramyltripeptide 127464-60-2, Vascular endothelial growth factor 139639-23-9, Tissue plasminogen activator 141436-78-4, Protein kinase C 143011-72-7, Granulocyte colony stimulating factor
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(device and methods for initiating chemical reactions and for targeted delivery of drugs or other agents)

IT **52-67-5**, Penicillamine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(device and methods for initiating chemical reactions and for targeted delivery of drugs or other agents)

RN 52-67-5 CAPLUS

CN D-Valine, 3-mercapto- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L38 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:298283 CAPLUS
DOCUMENT NUMBER: 136:74517
TITLE: Study on improvement of adhesion between gingival tissue and dental implant by collagen immobilization
AUTHOR(S): Norikawa, Noriyuki; Suzuki, Masakazu; Morita, Shinichiro; Yokoya, Shigetoshi; Miyamoto, Masatoshi; Fukuoka, Shinichi; Ozono, Satoru; Kinoshita, Yukihiko
CORPORATE SOURCE: Division of Research and Development, GUNZE Ltd., Inokura-shinmachi, Ayabe-shi, Kyoto, 623-8512, Japan
SOURCE: Seitai Zairyo (2001), 19(1), 10-20
CODEN: SEZAEH; ISSN: 0910-304X
PUBLISHER: Nippon Baiomateriaru Gakkai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB Few investigations concerned with the adhesion between dental implant and gingival tissue have been reported. If its adhesion is insufficient, bacterial plaque attaches onto the dental implant surface and induces an inflammatory cellular infiltration. As a result, alveolar bone is adsorbed and the transplanted implant is out of bone. The purpose of this study is to improve adhesive ability between gingival tissue and dental implant by the surface modification of titanium implants with collagen immobilization. Collagen could be immobilized onto the titanium surface using gold deposition and production of a stable monomol. layer with cysteine. Cell detaching expts. showed that cells strongly adhered on the collagen-immobilized surface compared with non-treated metal surfaces. Animal experiment was examined to evaluate effect of collagen immobilization onto the surface around Transmucosal Implant Extension (TIE), a part of com. available titanium dental implant, on adhesion against gingival tissue. In case of non-treated TIEs, bacterial plaque attached onto their surface, and down growth of gingival epithelium was observed In addition, even after 4 wks implantation, a moderate degree of inflammatory cellular infiltration was observed in the granulation tissue around the non-treated TIEs. On the other hand, a slight degree of inflammatory cellular infiltration was observed in the connective tissue around the most of them. After 4 wks implantation, in a part of them, collagen fibers had grown perpendicularly to the TIE surface to form a tight connection at the interface between gingival tissue and collagen-immobilized TIE. It is concluded that the collagen immobilization onto the dental implant surface would improve the adhesion against gingival tissue.

CC **63-7** (Pharmaceuticals)
Section cross-reference(s): 1

IT **Collagens, biological studies**
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); PYP (Physical process); **RCT (Reactant)**; THU (Therapeutic use); BIOL (Biological study); PROC (Process); **RACT (Reactant or reagent)**; USES (Uses)

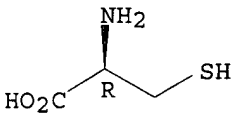
(type I; improvement of adhesion between gingival tissue and dental implant by collagen immobilization)

IT **52-90-4**, Cysteine, biological studies 7440-32-6, Titanium, biological studies
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); PYP (Physical process); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent); USES (Uses)
(improvement of adhesion between gingival tissue and dental implant by collagen immobilization)

IT **52-90-4**, Cysteine, biological studies
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); PYP (Physical process); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent); USES (Uses)
(improvement of adhesion between gingival tissue and dental implant by collagen immobilization)

RN 52-90-4 CAPLUS
CN L-Cysteine (9CI) (CA INDEX NAME)

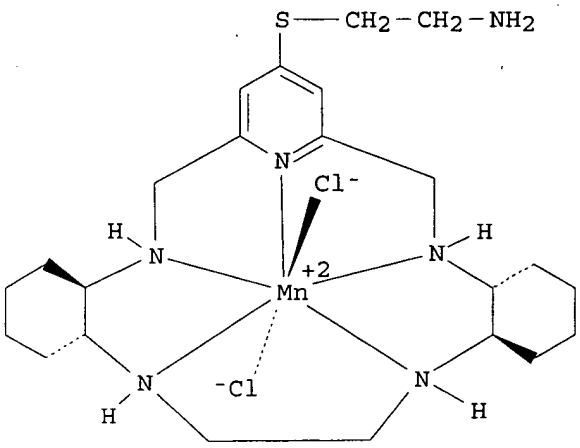
Absolute stereochemistry.



L38 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:861532 CAPLUS
DOCUMENT NUMBER: 134:33055
TITLE: Biomaterials modified with superoxide dismutase mimics
INVENTOR(S): Ornberg, Richard; Udipi, Kishore; Forster, Dennis; Riley, Dennis; Thurmond, Bruce; Henke, Susan; Brethaur, Kerry; Joardar, Saikat
PATENT ASSIGNEE(S): Monsanto Company, USA
SOURCE: PCT Int. Appl., 244 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000072893	A2	20001207	WO 2000-US14847	20000526
WO 2000072893	A3	20010830		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1185312	A2	20020313	EP 2000-932810	20000526
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

JP 2003500174 T2 20030107 JP 2000-620999 20000526
PRIORITY APPLN. INFO.: US 1999-136298P P 19990527
WO 2000-US14847 W 20000526
OTHER SOURCE(S): MARPAT 134:33055
GI



I

AB The present invention relates to biomaterials modified with non-proteinaceous catalysts for the dismutation of superoxide, and processes for making such materials. This modification may be by covalent conjugation, copolymn., or admixt. of the non-proteinaceous catalysts with the biomaterial. The resulting modified biomaterials exhibit a marked decrease in inflammatory response and subsequent degradation when placed in contact with vertebrate biol. systems. I was prepared as a catalyst and was conjugated with a number of polymers.

IC ICM A61L027-00
CC **63-8** (Pharmaceuticals)
Section cross-reference(s): 24, 35, 78
IT **Collagens, biological studies**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**reaction** products, with pentaazacyclopentadecane complexes; biomaterials modified with superoxide dismutase mimics)
IT **60-23-1**, 2-**Mercaptoethylamine** 107-22-2, Glyoxal 138-60-3, Chelidamic acid 1129-30-2, 2,6-Diacetylpyridine 5431-44-7, 2,6-Pyridinedicarboxaldehyde 20439-47-8, 1R,2R-Cyclohexanediamine 25038-59-9, Polyethylene terephthalate, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(biomaterials modified with superoxide dismutase mimics)
IT **60-23-1**, 2-**Mercaptoethylamine**
RL: RCT (Reactant); RACT (Reactant or reagent)
(biomaterials modified with superoxide dismutase mimics)
RN 60-23-1 CAPLUS
CN Ethanethiol, 2-amino- (8CI, 9CI) (CA INDEX NAME)

$H_2N—CH_2—CH_2—SH$

L38 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:628178 CAPLUS
DOCUMENT NUMBER: 133:213243
TITLE: Collagen peptides modified by grafting **mercapto** functions for use as biomaterials
INVENTOR(S): Nicolas, Florence; Bryson, Nathan
PATENT ASSIGNEE(S): Flamel Technologies, Fr.
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

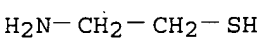
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000052052	A1	20000908	WO 2000-FR513	20000301
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2790475	A1	20000908	FR 1999-2727	19990302
FR 2790475	B1	20030124		
EP 1157039	A1	20011128	EP 2000-907750	20000301
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002541070	T2	20021203	JP 2000-602276	20000301

PRIORITY APPLN. INFO.: FR 1999-2727 A 19990302
WO 2000-FR513 W 20000301

AB The invention relates to novel collagen peptides that are modified by grafting free or substituted thiol functions carried by mercaptoamine radicals. The aim of the invention is to provide thiol collagens that can be crosslinked in a sufficient and controlled manner by forming S-S bridges and which are biocompatible. This is achieved by means of the inventive thiol collagens which are characterized in that the mercaptoamine radicals are identical to or different from each other and are exclusively grafted on the aspartic and glutamic acids of the collagen chain by amide bonds. The invention also relates to a method for the production of said thiol and crosslinkable collagens . The novel modified crosslinkable and/or crosslinked collagens can be used as biomaterials. Carboxylic acids of a peptide collagen were substituted by cysteine-Et ester. The above collagen peptide was crosslinked by hydrogen peroxide and was used to make a film which had dry thickness of 45 μm, maximum force at rupture of 2.9 N, elongation of 43%, and initial module of 4.6 MPa.

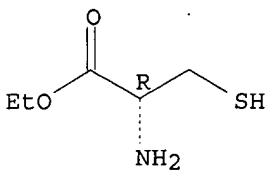
IC ICM C07K014-78
ICS C07K001-107; A61L024-10; A61L027-24; A61L015-32
CC **63-7** (Pharmaceuticals)
Section cross-reference(s): 38
ST collagen peptide **mercapto** function biomaterial film
IT **Collagens, reactions**
RL: **RCT (Reactant); RACT (Reactant or reagent)**
(atelocollagens; collagen peptides modified by grafting **mercapto** functions for use as biomaterials)

IT Microcapsules
Prosthetic materials and Prosthetics
(collagen peptides modified by grafting **mercapto** functions for use as biomaterials)
IT **Collagens, reactions**
RL: **RCT (Reactant); RACT (Reactant or reagent)**
(collagen peptides modified by grafting **mercapto** functions for use as biomaterials)
IT Medical goods
(dressings; collagen peptides modified by grafting **mercapto** functions for use as biomaterials)
IT Medical goods
Medical goods
(films; collagen peptides modified by grafting **mercapto** functions for use as biomaterials)
IT Prosthetic materials and Prosthetics
(implants; collagen peptides modified by grafting **mercapto** functions for use as biomaterials)
IT Films
Films
(medical; collagen peptides modified by grafting **mercapto** functions for use as biomaterials)
IT Animal tissue culture
(supports; collagen peptides modified by grafting **mercapto** functions for use as biomaterials)
IT Medical goods
(sutures; collagen peptides modified by grafting **mercapto** functions for use as biomaterials)
IT **60-23-1**, Cysteamine **3411-58-3**, Cysteine ethyl ester
7722-84-1, Hydrogen peroxide, reactions **92451-01-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(collagen peptides modified by grafting **mercapto** functions for use as biomaterials)
IT **60-23-1**, Cysteamine **3411-58-3**, Cysteine ethyl ester
92451-01-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(collagen peptides modified by grafting **mercapto** functions for use as biomaterials)
RN 60-23-1 CAPLUS
CN Ethanethiol, 2-amino- (8CI, 9CI) (CA INDEX NAME)



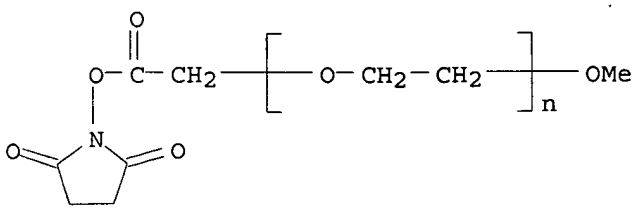
RN 3411-58-3 CAPLUS
CN L-Cysteine, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 92451-01-9 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[2-[(2,5-dioxo-1-pyrrolidinyl)oxy]-2-

oxoethyl]-ω-methoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:628042 CAPLUS
DOCUMENT NUMBER: 133:198753
TITLE: Crosslinked collagen peptide for preventing post-surgical adhesions
INVENTOR(S): Constancis, Alain; Meyrueix, Remi
PATENT ASSIGNEE(S): Flamel Technologies, Fr.
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000051661	A1	20000908	WO 2000-FR514	20000301
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2790391	A1	20000908	FR 1999-2728	19990302
FR 2790391	B1	20021115		
EP 1156839	A1	20011128	EP 2000-909403	20000301
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

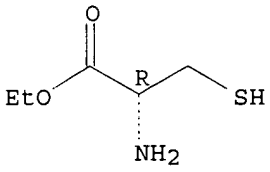
PRIORITY APPLN. INFO.: FR 1999-2728 A 19990302
WO 2000-FR514 W 20000301

AB The aim of the invention is to provide a means for preventing post-operative adhesions that is non-toxic, economic, in addition to being easy to obtain, sterilize, manipulate and implement, having controlled biodegradability and presenting a sufficiently strong initial mech. resistance in situ (cohesion). This is achieved in the case of said means for preventing post-operative adhesions and the invention is characterized in that it comprises at least one collagen peptide that is modified by grafting thiol functions that are free or substituted, cross-linkable and/or at least partly cross-linked, whereby the thiol functions are provided by mercaptoamine radicals that are exclusively grafted on the aspartic and glutamic acids of the collagen chains by means of amide bonds. The means can exist in the form of a homogeneous or composite

film, as a gel or in as a liquid which can be applied and cross-linked per se as on in vivo tissue. Carboxylic acids of a peptide collagen were substituted by cysteine-Et ester. The collagen was then crosslinked by iodine and used to prepare a film for prevention of post-surgical adhesions.

IC ICM A61L031-06
CC **63-7** (Pharmaceuticals)
Section cross-reference(s): 38
IT **Collagens, reactions**
RL: **RCT (Reactant); RACT (Reactant or reagent)**
(atelocollagens, type I and III; crosslinked collagen peptide for preventing post-surgical adhesions)
IT **Collagens, biological studies**
RL: DEV (Device component use); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crosslinked; crosslinked collagen peptide for preventing post-surgical adhesions)
IT **3411-58-3**, Cysteine-Ethyl ester 7553-56-2, Iodine, reactions
7722-84-1, Hydrogen peroxide, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(crosslinked collagen peptide for preventing post-surgical adhesions)
IT **3411-58-3**, Cysteine-Ethyl ester
RL: RCT (Reactant); RACT (Reactant or reagent)
(crosslinked collagen peptide for preventing post-surgical adhesions)
RN 3411-58-3 CAPLUS
CN L-Cysteine, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:458943 CAPLUS
DOCUMENT NUMBER: 131:78417
TITLE: Process for obtaining a natural nonsteroidal anabolic agent
INVENTOR(S): Serra, Helio Martins
PATENT ASSIGNEE(S): Brazil
SOURCE: Braz. Pedido PI, 17 pp.
CODEN: BPXXDX
DOCUMENT TYPE: Patent
LANGUAGE: Portuguese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BR 9701311	A	19981110	BR 1997-1311	19970317

PRIORITY APPLN. INFO.: BR 1997-1311 19970317
AB A process is disclosed for obtaining a nonsteroidal anabolic agent, which process involves taking a collagenous tissue (cow hide) immediately after

slaughter and submitting it to enzymic hydrolysis of protein. The cowhide obtained immediately after slaughter is cooked in a special reactor under pressure at 100-110°, at pH = 10-12 for 2 h. The material obtained is filtered and kept at 50-60°, then the filtrate is hydrolyzed with proteolytic enzymes (0.5-1%) for 6-10 h, at controlled temp and pH between 8-9, until hydrolysis is complete, obtaining a liquid hydrolyzate having a concentration of 10-15%. Further processing and sterilization with γ-radiation produces a product having an amino acid and mineral content specified in the invention.

IC ICM C07K014-78
ICS C07K001-12; A23L001-0562; A23J003-04; A23K001-165; A61K038-39

CC **63-3** (Pharmaceuticals)

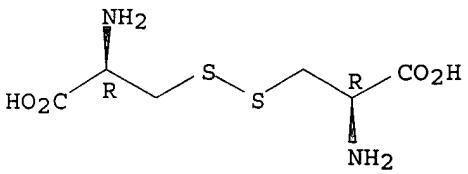
IT **Collagens, biological studies**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); **RCT (Reactant)**; THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PROC (Process); **RACT (Reactant or reagent)**; USES (Uses)
(process for obtaining a natural nonsteroidal anabolic agent)

IT 51-35-4P, Hydroxyproline 56-40-6P, Glycine, biological studies 56-41-7P, Alanine, biological studies 56-45-1P, Serine, biological studies 56-84-8P, Aspartic acid, biological studies 56-86-0P, Glutamic acid, biological studies 56-87-1P, Lysine, biological studies **56-89-3P**, Cystine, biological studies 60-18-4P, Tyrosine, biological studies 61-90-5P, Leucine, biological studies 63-68-3P, Methionine, biological studies 63-91-2P, Phenylalanine, biological studies 71-00-1P, Histidine, biological studies 72-18-4P, Valine, biological studies 72-19-5P, Threonine, biological studies 73-22-3P, Tryptophan, biological studies 73-32-5P, Isoleucine, biological studies 74-79-3P, L-Arginine, biological studies 77-92-9P, biological studies 147-85-3P, Proline, biological studies 1314-56-3P, Phosphorus pentoxide, biological studies 7439-89-6P, Iron, biological studies 7439-95-4P, Magnesium, biological studies 7439-96-5P, Manganese, biological studies 7440-23-5P, Sodium, biological studies 7440-42-8P, Boron, biological studies 7440-50-8P, Copper, biological studies 7440-66-6P, Zinc, biological studies 7440-70-2P, Calcium, biological studies 7632-50-0P, Ammonium citrate 7704-34-9P, Sulfur, biological studies 12136-45-7P, Potassium oxide, biological studies
RL: BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(process for obtaining a natural nonsteroidal anabolic agent)

IT **56-89-3P**, Cystine, biological studies
RL: BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(process for obtaining a natural nonsteroidal anabolic agent)

RN 56-89-3 CAPLUS
CN L-Cystine (9CI) (CA INDEX NAME)

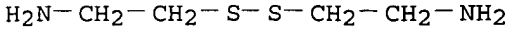
Absolute stereochemistry.



L38 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:363347 CAPLUS
DOCUMENT NUMBER: 127:86018
TITLE: Denatured **thiolated** collagen I. Synthesis and characterization
AUTHOR(S): Nicolas, Florence L.; Gagnieu, Christian H.
CORPORATE SOURCE: Equipe Biomateriaux, Laboratoire de Chimie Biologique, Institut National des Sciences Appliquees, Villeurbanne, 69621, Fr.
SOURCE: Biomaterials (1997), 18(11), 807-813
CODEN: BIMADU; ISSN: 0142-9612
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A new thiolating reagent is used to introduce sulfur groups into denatured atelocollagen. The procedure is easy to control and applicable on a large scale. The reagent is a reactive dicarboxylic acid compound containing sulfur in the form of a disulfide functionality. It is prepared by reacting N,N'-disuccinoylcystamine with 1,1'-carbonyldiimidazole. When this reagent is added to a solution of denatured atelocollagen in dimethylsulfoxide, amide bonds are formed between the carbonyl functions of the reagent and ε-NH2 of lysine and lhydroxylysine residues from the protein. The disulfide groups introduced can then be reduced by reaction with 1,4-dithiothreitol to give the -SH form of th modified protein. Control of the stoichiometry between the reagent and the protein can lead to varying modification levels. A maximum level of 0.33 mmol SH per g of protein can be attained, which corresponds to complete thiolation of the lysine and hydroxylysine residues. Thiolated denatured atelocollagen exhibits gelatin-like behavior, by being highly soluble in water at all pH values and by forming heat-reversible gels.

CC **63-7** (Pharmaceuticals)
ST **thiolation** collagen denatured
IT **Collagens, reactions**
RL: **RCT (Reactant); RACT (Reactant or reagent)**
(atelocollagens; preparation of denatured **thiolated** collagen)
IT **Collagens, biological studies**
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(denatured **thiolated**; preparation of denatured **thiolated** collagen)
IT Substitution reaction
(**thiolation**; preparation of denatured **thiolated** collagen)
IT 3483-12-3DP, 1,4-Dithiothreitol, reaction products with collagen derivative
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of denatured **thiolated** collagen)
IT **56-17-7**, Cystamine dihydrochloride 108-30-5, Succinic anhydride, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of denatured **thiolated** collagen)
IT 108725-86-6P 191794-44-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of denatured **thiolated** collagen)
IT **56-17-7**, Cystamine dihydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of denatured **thiolated** collagen)
RN 56-17-7 CAPLUS
CN Ethanamine, 2,2'-dithiobis-, dihydrochloride (9CI) (CA INDEX NAME)



L38 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:599239 CAPLUS
DOCUMENT NUMBER: 125:285010
TITLE: Method of preparing crosslinked polymeric biomaterial compositions for use in tissue augmentation
INVENTOR(S): Rhee, Woonza M.; Berg, Richard A.; Rosenblatt, Joel S.; Tefft, Jacqueline A.; Braga, Larry J.; Smestad, Thomas L.
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 14 pp., Cont.-in-part of U.S. Ser. No. 236,769.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 18
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5550187	A	19960827	US 1994-287549	19940808
US 5162430	A	19921110	US 1989-433441	19891114
US 5328955	A	19940712	US 1992-922541	19920730
US 5304595	A	19940419	US 1992-998802	19921230
US 5306500	A	19940426	US 1993-110577	19930823
US 5376375	A	19941227	US 1994-177578	19940105
US 5413791	A	19950509	US 1994-198128	19940217
US 5475052	A	19951212	US 1994-236769	19940502
US 5523348	A	19960604	US 1994-292415	19940818
US 5543441	A	19960806	US 1995-427576	19950424
US 5527856	A	19960618	US 1995-440274	19950512
US 5643464	A	19970701	US 1995-497573	19950630
EP 697218	A2	19960221	EP 1995-112218	19950803
EP 697218	A3	19960529		

R: DE, FR, GB, IT

PRIORITY APPLN. INFO.:

US 1988-274071	B2	19881121
US 1989-433441	A2	19891114
US 1992-922541	A3	19920730
US 1994-198128	A2	19940217
US 1994-236769	A2	19940502
US 1992-930142	A3	19920814
US 1993-110577	A3	19930823
US 1994-177578	A3	19940105
US 1994-287549	A3	19940808
US 1994-292415	A3	19940818
US 1995-497573	A	19950630

AB The present invention discloses a novel method for preparing crosslinked biomaterial compns. for use in the augmentation of soft or hard tissue. In general, the method comprises mixing a biocompatible polymer, which is preferably collagen, with a sterile, dry crosslinking agent, which is preferably a synthetic hydrophilic polymer such as a functionally activated polyethylene glycol. Also provided are preferred processes for

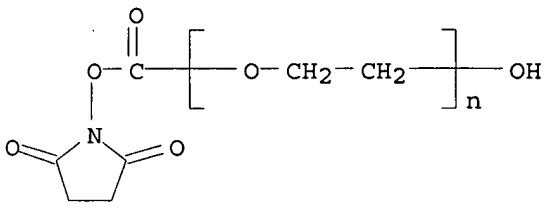
preparing sterile, dry crosslinking agents contained within syringes for use in the method of the invention. Methods for sterilization of the crosslinking agent include, but are not limited to, sterile filtration, aseptic processing, and e-beam or gamma irradiation Methods for providing augmentation of soft or hard tissue using crosslinked biomaterial compns. prepared according to the method of the invention are also disclosed. A sterile, dry crosslinking agent was prepared by mixing 1500 mg of disfunctionally activated PEG succinimidyl glutarate with 150 mL of water for injection and filtration sterilization using a Durapore filter; 0.5 mL of solution obtained was aliquotted into each of 180 3 cc syringes and lyophilized.

IC C08G063-49; C08G063-91
NCL 525054100
CC **63-7** (Pharmaceuticals)
Section cross-reference(s): 38
IT **Collagens, biological studies**
Glycosaminoglycans, biological studies
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); **RCT (Reactant)**; THU (Therapeutic use); BIOL (Biological study); PROC (Process); **RACT (Reactant or reagent)**; USES (Uses)
(crosslinking of; preparation of biopolymers crosslinked with activated polyethylene glycol as implant biomaterial for tissue augmentation)
IT Biopolymers
Collagens, biological studies
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(crosslinked, preparation of biopolymers crosslinked with activated polyethylene glycol as implant biomaterial for tissue augmentation)
IT **Collagens, biological studies**
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); **RCT (Reactant)**; THU (Therapeutic use); BIOL (Biological study); PROC (Process); **RACT (Reactant or reagent)**; USES (Uses)
(fibers, crosslinking of; preparation of biopolymers crosslinked with activated polyethylene glycol as implant biomaterial for tissue augmentation)
IT 25322-68-3DP, derivs., reaction products with biopolymers 26403-72-5DP, reaction products with collagen 62066-14-2DP, reaction products with collagen 151709-76-1DP, Polyethylene glycol propion aldehyde, reaction products with collagen 154467-38-6DP, Polyethylene glycol succinimidyl glutarate, reaction products with collagen **155919-13-4DP**, Polyethylene glycol succinimidyl carbonate, reaction products with collagen 159194-63-5DP, reaction products with collagen 182677-57-2DP, reaction products with collagen
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(preparation of biopolymers crosslinked with activated polyethylene glycol as implant biomaterial for tissue augmentation)
IT 26403-72-5 62066-14-2 151709-76-1, Polyethylene glycol propion aldehyde 154467-38-6, Polyethylene glycol succinimidyl glutarate **155919-13-4**, Polyethylene glycol succinimidyl carbonate 159194-63-5 182677-57-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of biopolymers crosslinked with activated polyethylene glycol as implant biomaterial for tissue augmentation)
IT **155919-13-4DP**, Polyethylene glycol succinimidyl carbonate, reaction products with collagen

RL: DEV (Device component use); PEP (Physical, engineering or chemical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(preparation of biopolymers crosslinked with activated polyethylene glycol as implant biomaterial for tissue augmentation)

RN 155919-13-4 CAPLUS

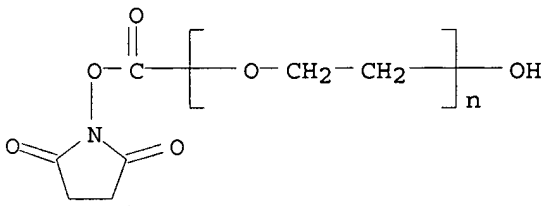
CN Poly(oxy-1,2-ethanediyl), α-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-ω-hydroxy- (9CI) (CA INDEX NAME)



IT **155919-13-4**, Polyethylene glycol succinimidyl carbonate
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of biopolymers crosslinked with activated polyethylene glycol as implant biomaterial for tissue augmentation)

RN 155919-13-4 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-ω-hydroxy- (9CI) (CA INDEX NAME)



L38 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:338359 CAPLUS

DOCUMENT NUMBER: 124:346521

TITLE: Biopolymers, especially collagens, modified by cysteine derivatives to permit crosslinking by formation of disulfide groups

INVENTOR(S): Bryson, Nathan

PATENT ASSIGNEE(S): Flamel Technologies, Fr.

SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9606880	A1	19960307	WO 1995-FR1117	19950824
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2723957	A1	19960301	FR 1994-10539	19940829
FR 2723957	B1	19970228		

PRIORITY APPLN. INFO.: FR 1994-10539 19940829

AB Collagens and gelatins are reacted with a cysteine derivative in which the thiol and amino groups are both protected by 1 group, e.g., 2,2-dimethyl-4-carboxythiazolidine in which the ring-completing protecting group is Me2C. The modified biopolymers are crosslinked by deprotection of thiol and amino groups and formation of disulfide crosslinks under mild conditions, e.g., in oxygenated water. The modified biopolymers are useful for medical implants, prostheses, etc.

IC ICM C08H001-06
ICS C09H007-00; A61L015-00; A61L027-00

CC 45-2 (Industrial Organic Chemicals, Leather, Fats, and Waxes)
Section cross-reference(s): **63**

IT Disulfide group
(preparation of biopolymer-carboxythiazolidine reaction products and deprotection of amino and **thiol** groups of thiazolidinecarbonyl groups to give cysteine residues suitable for crosslinking by formation of)

IT Crosslinking
(preparation of biopolymer-carboxythiazolidine reaction products and deprotection of amino and **thiol** groups of thiazolidinecarbonyl groups to give cysteine residues suitable for crosslinking by formation of disulfide bonds)

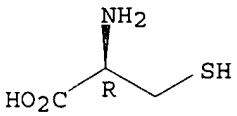
IT **Collagens, preparation**
Gelatins, preparation
RL: IMF (Industrial manufacture); PEP (Physical, engineering or chemical process); PREP (Preparation); PROC (Process)
(**reaction** products with carboxythiazolidines; preparation and deprotection of amino and **thiol** groups of thiazolidinecarbonyl groups to give cysteine residues suitable for crosslinking by formation of disulfide bonds)

IT **52-90-4DP**, Cysteine, derivs., reaction products with collagens and gelatins 444-27-9DP, 4-Thiazolidinecarboxylic acid, reaction products with collagens and gelatins 42607-20-5DP, 2,2-Dimethyl-4-thiazolidinecarboxylic acid, reaction products with collagens and gelatins
RL: IMF (Industrial manufacture); PEP (Physical, engineering or chemical process); PREP (Preparation); PROC (Process)
(preparation and deprotection of amino and **thiol** groups of thiazolidinecarbonyl groups to give cysteine residues suitable for crosslinking by formation of disulfide bonds)

IT **52-90-4DP**, Cysteine, derivs., reaction products with collagens and gelatins
RL: IMF (Industrial manufacture); PEP (Physical, engineering or chemical process); PREP (Preparation); PROC (Process)
(preparation and deprotection of amino and **thiol** groups of thiazolidinecarbonyl groups to give cysteine residues suitable for crosslinking by formation of disulfide bonds)

RN 52-90-4 CAPLUS
CN L-Cysteine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L38 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:886184 CAPLUS

DOCUMENT NUMBER: 123:266111
TITLE: Collagen-synthetic polymer conjugates having controlled fiber size distributions
INVENTOR(S): Rhee, Woonza M.
PATENT ASSIGNEE(S): Collagen Corp., USA
SOURCE: Eur. Pat. Appl., 40 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

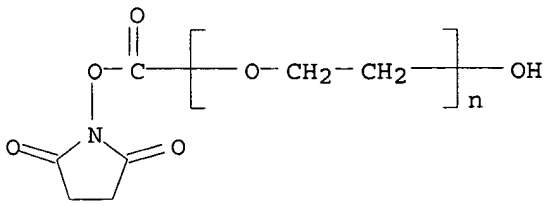
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 668081	A2	19950823	EP 1995-101927	19950213
EP 668081	A3	19960403		
R: AT, CH, DE, ES, FR, GB, IT, LI, SE				
AU 9510146	A1	19950824	AU 1995-10146	19950111
CA 2140108	AA	19950818	CA 1995-2140108	19950112
JP 08034857	A2	19960206	JP 1995-29647	19950217

PRIORITY APPLN. INFO.: US 1994-201860 19940217

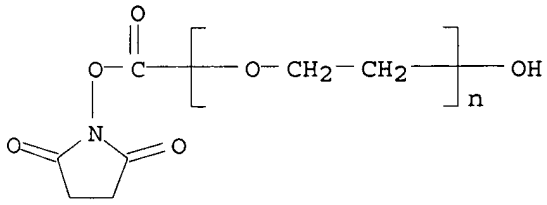
AB Current com. available fibrillar collagen compns. tend to have heterogeneous fiber size populations, including very large fibers, which are not conducive to efficient crosslinking using chemical crosslinking agents. The present invention disclosed preferred methods for producing collagens having relatively homogeneous, controlled fiber size populations, which are covalently conjugated to synthetic hydrophilic polymers, such as functionally activated polymeric glycols, to produce collagen-synthetic polymer conjugates having unique phys. and chemical characteristics. The resulting conjugates are used to prepare formed implants or injectable formulations for use in a variety of therapeutic applications. Compns. of the conjugates may include addnl. components, such as pharmaceutically acceptable fluid carriers and/or biol. active mols. such as growth factor or cytokines.

IC ICM A61L027-00
ICS C08L089-06; C08G081-00; C08H001-06
CC **63-6** (Pharmaceuticals)
Section cross-reference(s): 34, 38
IT **Collagens, reactions**
RL: **RCT (Reactant); RACT (Reactant or reagent)**
(atelo-, collagen-polymer conjugates with controlled fiber size for implants)
IT **Collagens, biological studies**
RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(atelo-, conjugates, collagen-polymer conjugates with controlled fiber size for implants)
IT 25322-68-3DP, Polyethylene glycol, conjugates with collagen
155919-13-4DP, Polyethylene glycol succinimidyl carbonate, conjugates with collagen
RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(collagen-polymer conjugates with controlled fiber size for implants)
IT **155919-13-4**, Polyethylene glycol succinimidyl carbonate
RL: RCT (Reactant); RACT (Reactant or reagent)
(collagen-polymer conjugates with controlled fiber size for implants)
IT **155919-13-4DP**, Polyethylene glycol succinimidyl carbonate, conjugates with collagen
RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(collagen-polymer conjugates with controlled fiber size for implants)
RN 155919-13-4 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-ω-hydroxy- (9CI) (CA INDEX NAME)



IT **155919-13-4**, Polyethylene glycol succinimidyl carbonate
RL: RCT (Reactant); RACT (Reactant or reagent)
(collagen-polymer conjugates with controlled fiber size for implants)
RN 155919-13-4 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]-ω-hydroxy- (9CI) (CA INDEX NAME)



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L38 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:410382 CAPLUS
DOCUMENT NUMBER: 122:170266
TITLE: Collagen derivatives containing **thiol** group as biomaterial for preparation of prostheses and implants
INVENTOR(S): Gagnieu, Christian; Nicolas, Florence; Soula, Gerard
PATENT ASSIGNEE(S): Flamel Technologies, Fr.
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9413731	A1	19940623	WO 1993-FR1258	19931216
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2699184	A1	19940617	FR 1992-15429	19921216
FR 2699184	B1	19950310		
EP 674677	A1	19951004	EP 1994-902824	19931216
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				

JP 08504463	T2	19960514	JP 1993-513893	19931216
US 5763579	A	19980609	US 1995-454189	19950616
PRIORITY APPLN. INFO.:			FR 1992-15429	19921216
			WO 1993-FR1258	19931216

OTHER SOURCE(S): MARPAT 122:170266

AB A modified collagen, which is soluble in water and/or in aprotic polar organic solvents and which comprises cysteine residue or derivs. thereof, directly grafted to the collagen chain, is prepared The ratio of free or substituted thiol groups is > 0.3, preferably > 0.5 mM/g, of collagen. The collagen derivs. are used for the preparation of biomaterials, particularly for the fabrication of implants and prostheses. A solution of N,N'-dibenzyloxycarbonyl-cysteine (preparation given) which was activated by pivaloyl chloride was reacted with a solution of collagen to obtain the collagen derivative which was precipitated, dialyzed at pH = 3, and lyophilized.

IC ICM C08H001-06
ICS A61L015-00; A61L027-00

CC **63-7** (Pharmaceuticals)
Section cross-reference(s): 34

ST collagen **thiol** deriv biomaterial prosthesis implant; cystein collagen deriv prepn prosthesis implant

IT Prosthetic materials and Prosthetics
Solvents
(collagen derivs. containing **thiol** group as biomaterial for preparation of prostheses and implants)

IT **Collagens, biological studies**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(collagen derivs. containing **thiol** group as biomaterial for preparation of prostheses and implants)

IT Solvents
(aprotic, collagen derivs. containing **thiol** group as biomaterial for preparation of prostheses and implants)

IT Skin
(artificial, collagen derivs. containing **thiol** group as biomaterial for preparation of prostheses and implants)

IT **Collagens, reactions**
RL: **RCT (Reactant); RACT (Reactant or reagent)**
(atelo-, collagen derivs. containing **thiol** group as biomaterial for preparation of prostheses and implants)

IT **Collagens, biological studies**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crosslinked, collagen derivs. containing **thiol** group as biomaterial for preparation of prostheses and implants)

IT Medical goods
(dressings, collagen derivs. containing **thiol** group as biomaterial for preparation of prostheses and implants)

IT Pharmaceutical dosage forms
(implants, collagen derivs. containing **thiol** group as biomaterial for preparation of prostheses and implants)

IT **52-90-4**, Cysteine, reactions 60-24-2, β-**Mercaptoethanol** 501-53-1, Benzylchloroformate 554-68-7 3282-30-2, Pivaloyl chloride 3483-12-3, Dithiothreitol 51507-96-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(collagen derivs. containing **thiol** group as biomaterial for preparation of prostheses and implants)

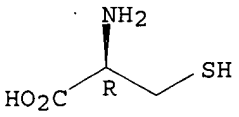
IT 6968-11-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(collagen derivs. containing **thiol** group as biomaterial for preparation of prostheses and implants)

IT **52-90-4**, Cysteine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(collagen derivs. containing **thiol** group as biomaterial for preparation of prostheses and implants)

RN 52-90-4 CAPLUS
CN L-Cysteine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L38 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:267108 CAPLUS
DOCUMENT NUMBER: 122:32395
TITLE: Biologically inert, biocompatible polymer conjugates
INVENTOR(S): Rhee, Woonza; Wallace, Donald G.; Michaels, Alan S.; Burns, Ramon A., Jr.; Fries, Louis; DeLustro, Frank; Bentz, Hanne
PATENT ASSIGNEE(S): Collagen Corp., USA
SOURCE: U.S., 22 pp. Cont.-in-part of U.S. 5,162,430.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 18
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5324775	A	19940628	US 1992-907518	19920702
US 5162430	A	19921110	US 1989-433441	19891114
CA 2003538	AA	19900521	CA 1989-2003538	19891121
CA 2003538	C	20010206		
JP 2505312	B2	19960605	JP 1989-501327	19891121
AT 168708	E	19980815	AT 1990-901254	19891121
ES 2119743	T3	19981016	ES 1990-901254	19891121
US 5264214	A	19931123	US 1992-930142	19920814
US 5304595	A	19940419	US 1992-998802	19921230
WO 9401483	A1	19940120	WO 1993-US6292	19930701
W: AU, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9346620	A1	19940131	AU 1993-46620	19930701
AU 677789	B2	19970508		
EP 648239	A1	19950419	EP 1993-916926	19930701
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08502082	T2	19960305	JP 1993-503427	19930701
US 5306500	A	19940426	US 1993-110577	19930823
US 5510418	A	19960423	US 1993-146843	19931103
US 5376375	A	19941227	US 1994-177578	19940105
US 5523348	A	19960604	US 1994-292415	19940818
US 5543441	A	19960806	US 1995-427576	19950424
US 5470911	A	19951128	US 1995-433656	19950504
US 5476666	A	19951219	US 1995-434725	19950504

PRIORITY APPLN. INFO.: US 1988-274071 B2 19881121

US 1989-433441	A2	19891114
US 1992-907518	A	19920702
US 1992-922541	A	19920730
US 1992-930142	A3	19920814
US 1992-984197	A	19921202
US 1992-984933	A	19921202
US 1992-985680	A	19921202
US 1993-25032	A	19930302
WO 1993-US6292	A	19930701
US 1993-110577	A3	19930823
US 1993-146843	A3	19931103
US 1994-177578	A3	19940105
US 1994-292415	A3	19940818

AB Pharmaceutically acceptable, non-immunogenic compns. are formed by covalently binding biol. inactive, natural, biocompatible polymer to pharmaceutically pure, synthetic, hydrophilic polymers via specific types of chemical bonds to provide biocompatible conjugates. The synthetic hydrophilic polymer may be PEG and derivs. thereof having a weight-average mol. weight 100-20,000. The compns. may include other components such as liquid pharmaceutically acceptable, carriers to form injectable formulations, and/or biol. active proteins such as growth factors. The conjugates of the invention generally contain large amts. of water when formed. The conjugates can be dehydrated to form a relatively solid object. The dehydrated, solid object can be ground into particles which can be suspended in a non-aqueous fluid such as an oil and injected into a living (preferably human) being for the purpose of providing soft tissue augmentation. Once in place, the particles rehydrate and expand in size five fold or more. Thus, reaction of PEG mono-Me ether with glutaric anhydride, reaction of the resulting acid ester with N-hydroxysuccinimide, and reaction of the resulting product with collagen gave a product with solid, coherent elasticity.

IC ICM C08G063-48
ICS C08G063-91; C08G063-40

NCL 525054200

CC 35-8 (Chemistry of Synthetic High Polymers)
Section cross-reference(s): **63**

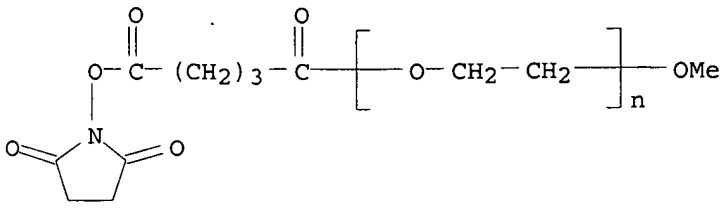
IT **Collagens, preparation**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(type I, **reaction** products, with PEG derivs.; biol. inert biocompatible polymer conjugates)

IT **111575-54-3P** 154467-38-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with collagen)

IT **111575-54-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction with collagen)

RN 111575-54-3 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,5-dioxopentyl]-ω-methoxy- (9CI) (CA INDEX NAME)



L38 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:708312 CAPLUS
DOCUMENT NUMBER: 121:308312
TITLE: Collagen-polymer conjugates for nonimmunogenic compositions and soft tissue augmentation
INVENTOR(S): Rhee, Woonza; Wallace, Donald G.; Michaels, Alan S.; Burns, Ramon A., Jr.; Fries, Louis; Delustro, Frank; Bentz, Hanne
PATENT ASSIGNEE(S): Collagen Corp., USA
SOURCE: U.S., 20 pp. Cont.-in-part of U.S. 5,162,430. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 18
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5328955	A	19940712	US 1992-922541	19920730
US 5162430	A	19921110	US 1989-433441	19891114
CA 2003538	AA	19900521	CA 1989-2003538	19891121
CA 2003538	C	20010206		
JP 2505312	B2	19960605	JP 1989-501327	19891121
AT 168708	E	19980815	AT 1990-901254	19891121
ES 2119743	T3	19981016	ES 1990-901254	19891121
US 5264214	A	19931123	US 1992-930142	19920814
US 5292802	A	19940308	US 1992-985680	19921202
US 5308889	A	19940503	US 1992-984197	19921202
US 5304595	A	19940419	US 1992-998802	19921230
WO 9401483	A1	19940120	WO 1993-US6292	19930701
W: AU, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9346620	A1	19940131	AU 1993-46620	19930701
AU 677789	B2	19970508		
EP 648239	A1	19950419	EP 1993-916926	19930701
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08502082	T2	19960305	JP 1993-503427	19930701
US 5306500	A	19940426	US 1993-110577	19930823
US 5565519	A	19961015	US 1993-147227	19931103
US 5376375	A	19941227	US 1994-177578	19940105
US 5413791	A	19950509	US 1994-198128	19940217
US 5475052	A	19951212	US 1994-236769	19940502
US 5550187	A	19960827	US 1994-287549	19940808
US 5523348	A	19960604	US 1994-292415	19940818
US 5446091	A	19950829	US 1995-368874	19950105
US 5543441	A	19960806	US 1995-427576	19950424
US 5527856	A	19960618	US 1995-440274	19950512
US 5643464	A	19970701	US 1995-497573	19950630
US 5936035	A	19990810	US 1995-573801	19951218

US 5800541 A 19980901 US 1997-780470 19970108
PRIORITY APPLN. INFO.: US 1988-274071 B2 19881121
US 1989-433441 A2 19891114
US 1992-907518 A 19920702
US 1992-922541 A2 19920730
US 1992-930142 A3 19920814
US 1992-984197 A 19921202
US 1992-984933 A 19921202
US 1992-985680 A 19921202
US 1993-25032 A 19930302
WO 1993-US6292 A 19930701
US 1993-110577 A3 19930823
US 1993-147227 B2 19931103
US 1994-177578 A3 19940105
US 1994-198128 A2 19940217
US 1994-198812 B1 19940218
US 1994-236769 A2 19940502
US 1994-287549 A3 19940808
US 1994-292415 A3 19940818
US 1995-440863 B1 19950515
US 1995-476825 A2 19950607

AB Pharmaceutically acceptable, nonimmunogenic compns. are formed by covalently binding atelopeptide collagens to pharmaceutically pure, synthetic, hydrophilic polymers via specific types of chemical bonds to provide collagen/polymer conjugates. The atelopeptide collagen can be type I, II, or III and may be fibrillar or nonfibrillar. The synthetic hydrophilic polymer may be polyethylene glycol and derivs. thereof having a weight average mol. weight 100-20,000. The compns. may include other components such as liquid, pharmaceutically acceptable carriers to form injectable formulations, and/or biol. active proteins such as growth factors. The collagen-polymer conjugates of the invention generally contain large amts. of water when formed. The conjugates can be dehydrated to form a relatively solid object. The dehydrated, solid object can be ground into particles which can be suspended in a nonaq. fluid such as an oil and injected for the purpose of providing soft tissue augmentation. Once in place, the particles rehydrate and expand in size five fold or more. For example, difunctional PEG succinimidyl glutarate was prepared and treated with collagen solution to obtain a microgel of random size fibrils.

IC ICM C08G063-48
ICS A61F013-00; A61F002-00
NCL 525054100
CC **63-6** (Pharmaceuticals)

IT **Collagens, biological studies**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(atelo-, collagen-polymer conjugates for nonimmunogenic compns. and soft tissue augmentation)

IT **Collagens, reactions**
RL: **RCT (Reactant); RACT (Reactant or reagent)**
(type I, collagen-polymer conjugates for nonimmunogenic compns. and soft tissue augmentation)

IT **Collagens, biological studies**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type I, conjugates, collagen-polymer conjugates for nonimmunogenic compns. and soft tissue augmentation)

IT **Collagens, biological studies**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type II, conjugates, collagen-polymer conjugates for nonimmunogenic compns. and soft tissue augmentation)

IT **Collagens, biological studies**

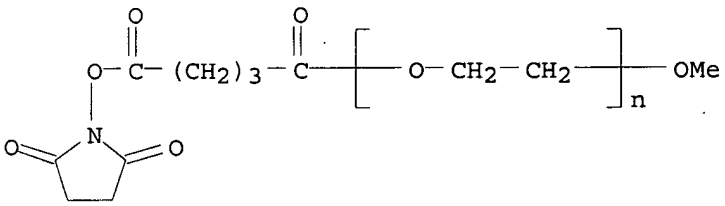
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type III, conjugates, collagen-polymer conjugates for nonimmunogenic compns. and soft tissue augmentation)

IT **111575-54-3DP**, collagen conjugates
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(collagen-polymer conjugates for nonimmunogenic compns. and soft tissue augmentation)

IT **111575-54-3DP**, collagen conjugates
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(collagen-polymer conjugates for nonimmunogenic compns. and soft tissue augmentation)

RN 111575-54-3 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α-[5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,5-dioxopentyl]-ω-methoxy- (9CI) (CA INDEX NAME)



L38 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:613038 CAPLUS
DOCUMENT NUMBER: 121:213038
TITLE: Crosslinkable derivatives of collagen, process for their preparation, and their use in the preparation of biomaterials for prostheses or other medical articles
INVENTOR(S): Gagnieu, Christian
PATENT ASSIGNEE(S): Flamel Technologies, S. A., Fr.
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 575273	A1	19931222	EP 1993-420255	19930617
EP 575273	B1	19971203		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
FR 2692582	A1	19931224	FR 1992-7692	19920618
FR 2692582	B1	19980918		
US 5412076	A	19950502	US 1993-77605	19930617
AT 160798	E	19971215	AT 1993-420255	19930617
ES 2113511	T3	19980501	ES 1993-420255	19930617
JP 06080935	A2	19940322	JP 1993-148108	19930618

PRIORITY APPLN. INFO.: FR 1992-7692 19920618

AB Crosslinkable collagens are disclosed which are soluble in water and/or aprotic polar organic solvents; the collagens have a free or substituted thiol function on residues of cysteine or derivs. thereof (homocysteine, cysteamine, etc.), the residues being bonded to collagen at least in part via a spacer compd (e.g. a dicarboxylic acid). Preparation of the modified

collagens is also provided. The modified collagens are useful for biomaterials for medical articles (prostheses, implants, etc.). Thus, a cysteaminyl succinyl collagen was prepared using bovine atelocollagen types I and III and disuccinylcystamine. The product was used in the formulation of a gel and of a film. Ex vivo evaluation of tissue adhesion (with rabbit muscle tissue) using a product of the invention is also described.

IC ICM C08H001-06
ICS A61L015-32; A61L025-00; A61L027-00

CC **63-7** (Pharmaceuticals)

ST crosslinkable collagen **thiol** deriv prepn; medical article crosslinkable collagen **thiol** deriv; prosthetic crosslinkable collagen **thiol** deriv; implant crosslinkable collagen **thiol** deriv; biomaterial crosslinkable collagen **thiol** deriv

IT Surgery
(adhesives for, crosslinkable collagen **thiol** derivs. for)

IT Gels
(crosslinkable collagen **thiol** derivative for, for medical article)

IT Medical goods
Prosthetic materials and Prosthetics
(crosslinkable collagen **thiol** derivs. for)

IT **Mercapto** group
(crosslinkable modified collagens with, preparation of, for biomaterial for prosthetic or other medical article)

IT Coating materials
(for prostheses, crosslinkable collagen **thiol** derivs. for)

IT **Collagens, preparation**
RL: PREP (Preparation)
(**thiol**-modified, crosslinkable, preparation of, for biomaterial for prosthetic or other medical article)

IT Skin
(artificial, crosslinkable collagen **thiol** derivs. for)

IT **Collagens, reactions**
RL: **RCT (Reactant)**; **RACT (Reactant or reagent)**
(atelo-, **reaction** of, in crosslinkable collagen **thiol** derivative preparation for biomaterial for prosthetic or other medical article)

IT **Collagens, uses**
RL: **RCT (Reactant)**; SPN (Synthetic preparation); PREP (Preparation); **RACT (Reactant or reagent)**
(atelo-, succinylated, preparation and **reaction** of, in crosslinkable collagen **thiol** derivative preparation for biomaterial for prosthetic or other medical article)

IT Adhesives
(biol., crosslinkable collagen **thiol** derivs. for)

IT Medical goods
(dressings, crosslinkable collagen **thiol** derivs. for)

IT Medical goods
(films, crosslinkable collagen **thiol** derivative for)

IT Prosthetic materials and Prosthetics
(implants, crosslinkable collagen **thiol** derivs. for)

IT **Collagens, preparation**
RL: **RCT (Reactant)**; SPN (Synthetic preparation); PREP (Preparation); **RACT (Reactant or reagent)**
(succinylated, preparation and **reaction** of, in crosslinkable collagen **thiol** derivative preparation for biomaterial for prosthetic or other medical article)

IT **51-85-4DP**, Cystamine, collagen reaction products **52-90-4DP**

, Cysteine, collagen reaction products **52-90-4DP**, Cysteine, derivs., collagen reaction products **56-89-3DP**, Cystine, collagen reaction products **60-23-1DP**, Cysteamine, collagen reaction products 88-99-3DP, 1,2-Benzenedicarboxylic acid, derivs., reaction products with collagen and cysteine (derivative) 88-99-3DP, 1,2-Benzenedicarboxylic acid, reaction products with collagen and cysteine (derivative) 97-65-4DP, Itaconic acid, derivs., reaction products with collagen and cysteine (derivative) 97-65-4DP, Itaconic acid, reaction products with collagen and cysteine (derivative) 110-15-6DP, Butanedioic acid, derivs., reaction products with collagen and cysteine (derivative) 110-15-6DP, Butanedioic acid, reaction products with collagen and cysteine (derivative) 110-16-7DP, 2-Butenedioic acid (Z)-, derivs., reaction products with collagen and cysteine (derivative) 110-16-7DP, 2-Butenedioic acid (Z)-, reaction products with collagen and cysteine (derivative) 110-94-1DP, Glutaric acid, derivs., reaction products with collagen and cysteine (derivative) 110-94-1DP, Glutaric acid, reaction products with collagen and cysteine (derivative) 462-10-2DP, Homocystine, collagen reaction products 498-23-7DP, Citraconic acid, derivs., reaction products with collagen and cysteine (derivative) 498-23-7DP, Citraconic acid, reaction products with collagen and cysteine (derivative) **6027-13-0DP**, Homocysteine, collagen reaction products
RL: PREP (Preparation)
(crosslinkable, preparation of, for biomaterial for prosthetic or other medical article)

IT 64949-90-2DP, reaction products with succinyl collagen
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deprotection of, in crosslinkable collagen **thiol** derivative preparation for biomaterial for prosthetic or other medical article)

IT 108-30-5DP, collagen reaction products
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in crosslinkable collagen **thiol** derivative preparation for biomaterial for prosthetic or other medical article)

IT **56-17-7DP**, Cystamine hydrochloride, reaction products with succinyl atelocollagen **1069-29-0DP**, Cystine dimethyl ester, reaction products with succinyl atelocollagen 62686-51-5DP, reaction products with atelocollagen 108725-86-6DP, collagen reaction products
RL: PREP (Preparation)
(preparation of, for crosslinkable collagen **thiol** derivative for biomaterial for prosthetic or other medical article)

IT **56-17-7**, Cystamine hydrochloride 108-30-5, reactions 110-15-6, Butanedioic acid, reactions **1069-29-0**, Cystine dimethyl ester 62686-51-5 64949-90-2 108725-86-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in crosslinkable collagen **thiol** derivative preparation for biomaterial for prosthetic or other medical article)

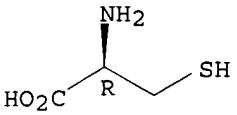
IT **51-85-4DP**, Cystamine, collagen reaction products **52-90-4DP**, Cysteine, collagen reaction products **56-89-3DP**, Cystine, collagen reaction products **60-23-1DP**, Cysteamine, collagen reaction products **6027-13-0DP**, Homocysteine, collagen reaction products
RL: PREP (Preparation)
(crosslinkable, preparation of, for biomaterial for prosthetic or other medical article)

RN 51-85-4 CAPLUS
CN Ethanamine, 2,2'-dithiobis- (9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-S-S-CH_2-CH_2-NH_2$

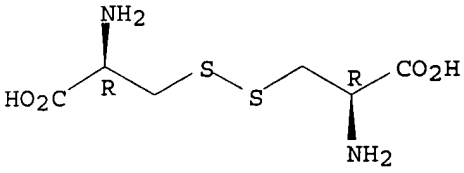
RN 52-90-4 CAPLUS
CN L-Cysteine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 56-89-3 CAPLUS
CN L-Cystine (9CI) (CA INDEX NAME)

Absolute stereochemistry.

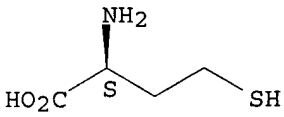


RN 60-23-1 CAPLUS
CN Ethanethiol, 2-amino- (8CI, 9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-SH$

RN 6027-13-0 CAPLUS
CN L-Homocysteine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



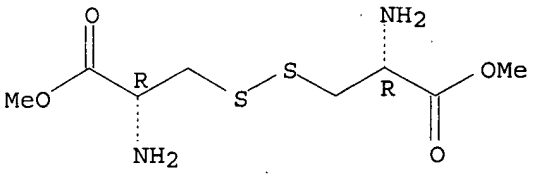
IT **56-17-7DP**, Cystamine hydrochloride, reaction products with succinyl atelocollagen **1069-29-0DP**, Cystine dimethyl ester, reaction products with succinyl atelocollagen
RL: PREP (Preparation)
(preparation of, for crosslinkable collagen **thiol** derivative for biomaterial for prosthetic or other medical article)
RN 56-17-7 CAPLUS
CN Ethanamine, 2,2'-dithiobis-, dihydrochloride (9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-S-S-CH_2-CH_2-NH_2$

●2 HCl

RN 1069-29-0 CAPLUS
CN L-Cystine, dimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



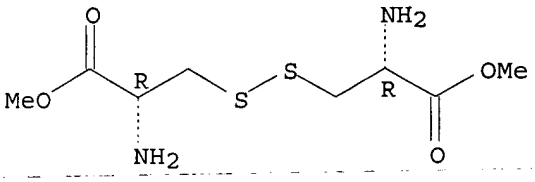
IT **56-17-7**, Cystamine hydrochloride **1069-29-0**, Cystine dimethyl ester
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in crosslinkable collagen **thiol** derivative preparation for biomaterial for prosthetic or other medical article)
RN 56-17-7 CAPLUS
CN Ethanamine, 2,2'-dithiobis-, dihydrochloride (9CI) (CA INDEX NAME)

$H_2N-CH_2-CH_2-S-S-CH_2-CH_2-NH_2$

●2 HCl

RN 1069-29-0 CAPLUS
CN L-Cystine, dimethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L38 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:587301 CAPLUS
DOCUMENT NUMBER: 121:187301
TITLE: Amino acids useful as inhibitors of the advanced glycosylation of proteins
INVENTOR(S): Ulrich, Peter C.; Cerami, Anthony
PATENT ASSIGNEE(S): Rockefeller University, USA; Alteon Inc.
SOURCE: U.S., 12 pp. Cont.-in-part of U.S. Ser. No. 805,200.
CODEN: USXXAM

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 33
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5334617	A	19940802	US 1992-825598	19920127
EP 322402	A2	19890628	EP 1989-102406	19850319
EP 322402	A3	19891025		
EP 322402	B1	19931124		
R: AT, BE, CH, DE, FR, GB, LI, LU, NL, SE				
AT 97741	E	19931215	AT 1989-102406	19850319
US 5100919	A	19920331	US 1990-606425	19901031
US 5126442	A	19920630	US 1991-638735	19910108
US 5238963	A	19930824	US 1991-805200	19911210
US 5254593	A	19931019	US 1991-807609	19911216
JP 05172813	A2	19930713	JP 1992-51657	19920310
US 5318982	A	19940607	US 1992-986661	19921208
WO 9313775	A1	19930722	WO 1993-US386	19930115
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9335840	A1	19930803	AU 1993-35840	19930115
WO 9314750	A2	19930805	WO 1993-US709	19930127
WO 9314750	A3	19931209		
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 624088	A1	19941117	EP 1993-904653	19930127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07503713	T2	19950420	JP 1993-513401	19930127
CA 2128248	C	19970701	CA 1993-2128248	19930127
US 5468777	A	19951121	US 1994-236228	19940429
US 5801200	A	19980901	US 1995-418525	19950407
US 5733933	A	19980331	US 1995-473009	19950607
US 5733524	A	19980331	US 1995-479673	19950607
US 5811075	A	19980922	US 1995-487398	19950607

PRIORITY APPLN. INFO.:

US 1984-590820	A2	19840319
US 1985-798032	A3	19851114
US 1988-220504	B2	19880717
US 1990-481869	A3	19900220
US 1991-805200	A2	19911210
EP 1989-102406	A	19850319
US 1986-907747	B2	19860912
US 1987-91534	A3	19870903
US 1989-453935	A3	19891220
US 1989-453958	B1	19891220
US 1990-606425	A3	19901031
US 1991-709487	B1	19910603
US 1992-822310	A	19920117
US 1992-825598	A	19920127
US 1992-878837	B1	19920505
US 1992-887279	B2	19920521
WO 1993-US386	A	19930115
WO 1993-US709	W	19930127
US 1993-29417	A2	19930311
US 1993-162840	B1	19931203
US 1994-236228	A2	19940429
US 1994-290680	B1	19940815
US 1994-319747	A2	19941007
US 1995-418525	A2	19950407

OTHER SOURCE(S): MARPAT 121:187301

AB The present invention relates to compns. and methods for inhibiting protein aging. Accordingly, a composition is disclosed which comprises an agent or compound capable of inhibiting the formation of advanced glycosylation end products of target proteins by reacting with the carbonyl moiety of the early glycosylation product of such target proteins formed by their initial glycosylation. Suitable agents are amino acids and their derivs. which contain an active nitrogen-containing group. Particular agents comprise lysine and mixts. thereof. The agents are effective for the treatment of complications of diabetes and aging caused by the accumulation of advanced glycosylation end-products in the body.

IC ICM A61K031-195

NCL 514562000

CC **63-5** (Pharmaceuticals)
Section cross-reference(s): 1

IT **Collagens, biological studies**
Elastins
Proteins, reactions
RL: **RCT (Reactant); RACT (Reactant or reagent)**
(advanced glycosylation of, inhibition of, with amino acids, for treatment of age-related diseases)

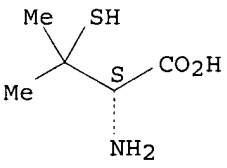
IT **52-67-5 52-89-1** 56-12-2, 4-Aminobutyric acid, biological studies 305-62-4, DL-2,4-Diaminobutyric acid 657-27-2, Lysine monohydrochloride 3184-13-2, L-Ornithine monohydrochloride
RL: BIOL (Biological study)
(protein advanced glycosylation inhibition with, aging and diabetes complications in relation to)

IT **52-67-5 52-89-1**
RL: BIOL (Biological study)
(protein advanced glycosylation inhibition with, aging and diabetes complications in relation to)

RN 52-67-5 CAPLUS

CN D-Valine, 3-mercapto- (9CI) (CA INDEX NAME)

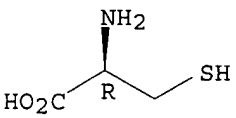
Absolute stereochemistry.



RN 52-89-1 CAPLUS

CN L-Cysteine, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L38 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:564053 CAPLUS
DOCUMENT NUMBER: 121:164053
TITLE: Dehydrated collagen-polymer strings
INVENTOR(S): Rhee, Woonza; Fries, Louis; Damani, Ramesh; Mccullough, Kimberly; Delustro, Frank
PATENT ASSIGNEE(S): Collagen Corp., USA
SOURCE: U.S., 24 pp. Cont.-in-part of U.S. Ser. No. 922,541. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 18
PATENT INFORMATION:

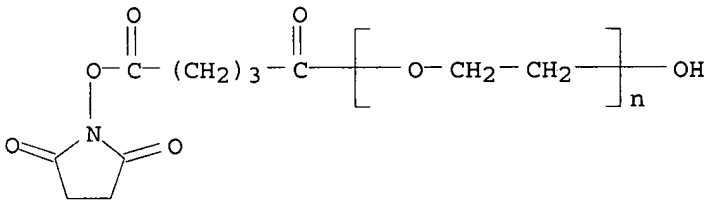
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5308889	A	19940503	US 1992-984197	19921202
US 5162430	A	19921110	US 1989-433441	19891114
US 5328955	A	19940712	US 1992-922541	19920730
US 5304595	A	19940419	US 1992-998802	19921230
WO 9401483	A1	19940120	WO 1993-US6292	19930701
W: AU, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9346620	A1	19940131	AU 1993-46620	19930701
AU 677789	B2	19970508		
EP 648239	A1	19950419	EP 1993-916926	19930701
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08502082	T2	19960305	JP 1993-503427	19930701
US 5306500	A	19940426	US 1993-110577	19930823
US 5376375	A	19941227	US 1994-177578	19940105
US 5523348	A	19960604	US 1994-292415	19940818
US 5543441	A	19960806	US 1995-427576	19950424

PRIORITY APPLN. INFO.:
US 1988-274071 B2 19881121
US 1989-433441 A2 19891114
US 1992-922541 A2 19920730
US 1992-907518 A 19920702
US 1992-930142 A3 19920814
US 1992-984197 A 19921202
US 1992-984933 A 19921202
US 1992-985680 A 19921202
US 1993-25032 A 19930302
WO 1993-US6292 A 19930701
US 1993-110577 A3 19930823
US 1994-177578 A3 19940105
US 1994-292415 A3 19940818

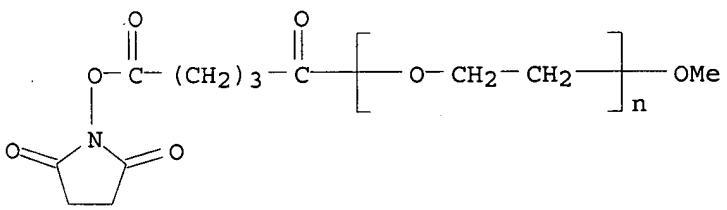
AB Medical articles in the form of strings are formed by covalently binding collagen to pharmaceutically pure, synthetic, hydrophilic polymers, such as PEG, via specific types of chemical bonds to provide collagen/polymer conjugate formulations which are extruded to make the strings. The string can be designed to incorporate other components such as fluid, pharmaceutically acceptable carriers to form injectable formulations, and/or biol. active proteins such as growth factors or cytokines. The strings contain large amts. of water when extruded and may then be dehydrated to form relatively solid but flexible strings. The strings can be injected into a living being for the purpose of providing soft tissue augmentation. Once in place, the strings rehydrate and expand in size five fold or more. Aqueous solution can be provided to enhance the rate of rehydration. The strings can also be used to suture wounds which strings can be chemical designed to dissolve in situ. Collagen solution was mixed with a solution of activated PEG succinimidyl glutarate (preparation given) and the

mixture was allowed to stand at 17-22° for 15 h, then it was centrifuged and the resulting pellet was collected and washed. The force required to extrude collagen-PEG conjugate through a 30 gauge needle was 8-10 as compared to 20-30 N for Zyderm collagen implant.

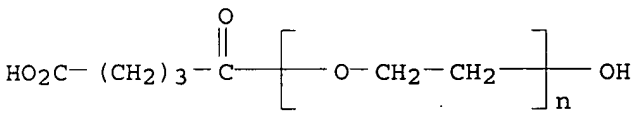
IC ICM C08G063-48
ICS C08G063-91; A61F002-00
NCL 523113000
CC **63-7** (Pharmaceuticals)
Section cross-reference(s): 35
IT **Collagens, reactions**
RL: **RCT (Reactant); RACT (Reactant or reagent)**
(reaction of, with PEG succinimidyl glutarate)
IT **Collagens, preparation**
RL: PREP (Preparation)
(atelo-, conjugates, with PEG, preparation of, for medical goods)
IT **Collagens, preparation**
RL: PREP (Preparation)
(conjugates, with PEG, preparation of, for medical goods)
IT **Collagens, preparation**
RL: PREP (Preparation)
(type I, conjugates with PEG, preparation of, for medical goods)
IT **108188-71-2P 111575-54-3P** 154467-38-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with collagen)
IT **95934-91-1P** 157598-59-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with hydroxysuccinimide)
IT **108188-71-2P 111575-54-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with collagen)
RN 108188-71-2 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,5-dioxopentyl]-ω-hydroxy- (9CI) (CA INDEX NAME)



RN 111575-54-3 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-[5-[(2,5-dioxo-1-pyrrolidinyl)oxy]-1,5-dioxopentyl]-ω-methoxy- (9CI) (CA INDEX NAME)



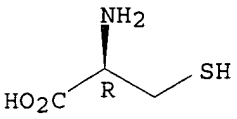
IT **95934-91-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with hydroxysuccinimide)
RN 95934-91-1 CAPLUS
CN Poly(oxy-1,2-ethanediyl), α-(4-carboxy-1-oxobutyl)-ω-hydroxy- (9CI) (CA INDEX NAME)



L38 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:1723 CAPLUS
DOCUMENT NUMBER: 120:1723
TITLE: Cloning, expression, and sequencing of a protease gene (tpr) from Porphyromonas gingivalis W83 in Escherichia coli
AUTHOR(S): Bourgeau, G.; Lapointe, H.; Peloquin, P.; Mayrand, D.
CORPORATE SOURCE: Fac. Sci. Genie, Univ. Laval, Quebec, QC, G1K 7P4, Can.
SOURCE: Infection and Immunity (1992), 60(8), 3186-92
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English
AB P. gingivalis is a highly proteolytic organism which metabolizes small peptides and amino acids. Indirect evidence suggests that the proteases produced by this microorganism constitute an important virulence factor. In this study, a gene bank of P. gingivalis W83 DNA was constructed by cloning 0.5- to 20-kb HindIII-cut DNA fragments into Escherichia coli DH5α by using the plasmid vector of pUC19. A clone expressing a protease from P. gingivalis was isolated on LB agar containing 1% skim milk. The clone contained a 3.0-kb insert that coded for a protease with an apparent mol. mass of 64 kDa. Sequencing part of the 3.0-kb DNA fragment revealed an open reading frame encoding a protein of 482 amino acids with a mol. mass of 62.5 kDa. Putative promoter and termination elements flanking the open reading frame were identified. The activity expressed in E. coli was extensively characterized by using various substrates and protease inhibitors, and the results suggest that it is possibly a thiol protease.
CC 3-3 (Biochemical Genetics)
Section cross-reference(s): 7, 10
IT **Collagens, reactions**
RL: **RCT (Reactant)**; **RACT (Reactant or reagent)**
(autoclave, as substrate for protease of Porphyromonas gingivalis)
IT **52-90-4**, Cysteine, biological studies
RL: BIOL (Biological study)
(protease of Porphyromonas gigivalis expressed in Escherichia coli stimulation by)
IT 60-24-2, 2-**Mercaptoethanol** 3483-12-3, Dithiothreitol
RL: PRP (Properties)
(protease of Porphyromonas gigivalis expressed in Escherichia coli stimulation by)
IT **52-90-4**, Cysteine, biological studies
RL: BIOL (Biological study)

(protease of Porphyromonas gigivalis expressed in Escherichia coli stimulation by)
RN 52-90-4 CAPLUS
CN L-Cysteine (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L38 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:567768 CAPLUS
DOCUMENT NUMBER: 119:167768
TITLE: Amino acids useful as inhibitors of the advanced glycosylation of proteins
INVENTOR(S): Ulrich, Peter C.; Cerami, Anthony
PATENT ASSIGNEE(S): Rockefeller University, USA; Alteon Inc.
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 33
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9314750	A2	19930805	WO 1993-US709	19930127
WO 9314750	A3	19931209		
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5126442	A	19920630	US 1991-638735	19910108
US 5334617	A	19940802	US 1992-825598	19920127
WO 9313775	A1	19930722	WO 1993-US386	19930115
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9335840	A1	19930803	AU 1993-35840	19930115
EP 624088	A1	19941117	EP 1993-904653	19930127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07503713	T2	19950420	JP 1993-513401	19930127

PRIORITY APPLN. INFO.:

US 1992-825598	A	19920127
US 1984-590820	A2	19840319
US 1985-798032	A3	19851114
US 1988-220504	B2	19880717
US 1989-453935	A3	19891220
US 1990-481869	A3	19900220
US 1991-805200	A2	19911210
US 1992-822310	A	19920117
WO 1993-US386	A	19930115
WO 1993-US709	W	19930127

OTHER SOURCE(S): MARPAT 119:167768
AB Amino acids and their derivs. are topically, parenterally, or orally administered to inhibit the protein aging by preventing formation of advanced glycosylation end products of target proteins such as collagens, blood vessel walls, and glomerular basement membranes. Therefore, they are useful in the treatment of diabetes complications, atherosclerosis, peripheral neuropathy, cataracts, etc. For example, administration of

aminoguanidine·HCl to diabetic rats prevented crosslinking of collagen in tail tendon fiber by .apprx.80%. Formulations containing amino acid derivs. are also given.

IC ICM A61K031-195

CC **63-6** (Pharmaceuticals)
Section cross-reference(s): 1

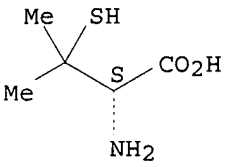
IT **Collagens, biological studies**
Elastins
RL: **RCT (Reactant); RACT (Reactant or reagent)**
(glycosylation of, amino acids for prevention of, in treatment of diseases associated with aging)

IT **52-67-5 52-89-1** 56-12-2, biological studies
305-62-4, DL-2,4-Diaminobutyric acid 657-27-2, L-Lysine monohydrochloride 921-52-8, 2,3-Diaminosuccinic acid 3184-13-2, L-Ornithine monohydrochloride
RL: BIOL (Biological study)
(diseases associated with protein aging treatment with)

IT **52-67-5 52-89-1**
RL: BIOL (Biological study)
(diseases associated with protein aging treatment with)

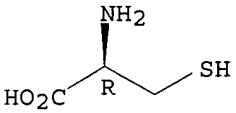
RN 52-67-5 CAPLUS
CN D-Valine, 3-mercapto- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 52-89-1 CAPLUS
CN L-Cysteine, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L38 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1979:422431 CAPLUS
DOCUMENT NUMBER: 91:22431
TITLE: Chemical modification of carboxyl group of bovine collagen fiber with carbodiimides
AUTHOR(S): Chonan, Yasumasa; Matsunaga, Ayako; Toyoda, Harukazu
CORPORATE SOURCE: Fac. Agric., Tokyo Noko Univ., Tokyo, Japan
SOURCE: Hikaku Kagaku (Chemistry) (1978), 24(3), 140-7
CODEN: HIKAAF; ISSN: 0018-1811
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB Carboxyl groups were modified with taurin [23522-05-6], ethylenediamine [107-15-3], or a similar nucleophilic reagent in the presence of an activator such as 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (I) [1892-57-5], N,N'-dicyclohexyl carbodiimide [538-75-0], and 1-cyclohexyl-3-(2-morpholinoethyl)carbodiimide methyl-p-toluenesulfonate [2491-17-0] and I was the most effective activator. A high extent of modification was observed at I-free carboxyl group molar ratio 35:1, pH .apprx.5, reaction temperature 20°, and reaction time 24 h, and, for example, >80% of the free carboxyl groups were modified with glycerin derivs. The fiber structure seemed to be unchanged during the modification.

CC 41-2 (Leather and Related Materials)

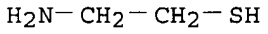
IT **Collagens, reactions**
RL: **RCT (Reactant); RACT (Reactant or reagent)**
(fibers, **reaction** of, with amines, in presence of carbodiimides)

IT **60-23-1** 75-04-7, reactions 107-15-3, reactions 141-43-5, reactions 459-73-4 598-41-4 4070-48-8 4540-60-7 23522-05-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with collagen fibers, in presence of carbodiimides)

IT **60-23-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with collagen fibers, in presence of carbodiimides)

RN 60-23-1 CAPLUS

CN Ethanethiol, 2-amino- (8CI, 9CI) (CA INDEX NAME)



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